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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,288	04/25/2001	Herwig Buchholz	MERCK 1943	7732

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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	7

DATE MAILED: 04/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,288	BUCHHOLZ ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-28* is/are pending in the application.

4a) Of the above claim(s) *7-11 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 14-23* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election Acknowledged

1. Applicants election with traverse the Group I, claims 1-6 and 14-23, is acknowledged. Applicants request that all three groups be examined during prosecution, or in the alternative request that upon prosecution, if the subject matter linking the three groups is found to contribute patentable subject matter to the art, that the claims of the non-elected groups be considered in the same application.

Applicants argument is deemed to be nonpersuasive since the technical feature linking claims, namely a composition comprising (a) a methyl or methylene donors (b) methyl transporter and (c) bioflavonoids is well known in the art evidenced by commercially available Product Maxi-Chel and Mega-Chel containing choline, methionine, folic acid and rutin as well as a composition disclosed in US 5198216 (e.g., Table Ib, IIb, IIIb). Therefore, the restriction is deemed proper and made Final.

Priority

2. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

New Ground of Rejection

3. This Office Action requires new ground of rejection necessitated by Amendment filed on July 10, 2002. The scope has been changed by the Amendment. The scope of the claimed subject matter that was originally filed was directed to a composition comprising one or more active ingredients, wherein the active ingredients selected from (a) a component A consisting of one or more compounds selected from methyl and methylene donors, (b) a component B consisting of

one or more methyl transporters and (c) a component C consisting of one or more bioflavonoids. However, the subject matter of the instant claims changed by the amendment requires a composition comprising all three components, a component A, B and C.

Claim Objections

4. Claim 20 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 6. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 5-6, 14-16, 20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by McGee (US 5198216).

McGee discloses a composition comprising (a) methyl or methylene donor such as choline and methionine, (b) methyl transporter such as folic acid (synonym: pteroyl-L-glutamic acid), (c) bioflavonoid such as rutin, nutritional substances (e.g., vitamin C, vitamin B1, B2, B6, B12, etc...) and auxiliaries (e.g., raw tissue concentrate of adrenal, raw tissue concentrate of pituitary, etc...), wherein said composition is prepared in powder or liquid form (Table Ib, IIb,

IIIb, Ivb, Vb and claim 16). McGee also discloses the claimed food or food supplement comprising said composition (column 3, lines 7-8).

Although McGee is silent about the functional characteristic of choline or methionine as methyl or methylene donor and folic acid as methyl transporter, such characteristic or property is deemed to be inherent to the composition. Thus, the reference anticipates the claimed invention.

6. Claims 1-2, 5-6, 14, 16, 20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Lockett (US 5626884).

Lockett discloses a composition comprising (a) methyl or methylene donor such as betaine and choline (in salt form), (b) methyl transporter such as folic acid (synonym: pteroyl-L-glutamic), (c) bioflavonoid such as rutin, nutritional substance (e.g., vitamin A, vitamin B1, B2, B6, B12, vitamin C, vitamin D, vitamin E, etc...), excipients or auxiliaries and carriers, wherein said composition is prepared in tablet or capsules (Example; column 4, lines 32-53; claims).

Although Lockett is silent about the functional characteristic of choline or betaine as methyl or methylene donor and folic acid as methyl transporter, such characteristic or property is deemed to be inherent to the composition. Thus, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 3-4, 17-19, 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockett (US 5626884) in view of Bailey et al. (US 5997915).

The teaching of Lockett has been discussed in above 35 USC 102(b) rejection.

The teaching of Lockett differs from the claimed invention in (i) the use of folic acid derivatives, namely 5-methyltetrahydrofolic acid, more specifically 5-methyl-(6S)-tetrahydrofolic acid (required in claims 3-4, 19, 21 and 23); (ii) "lyophilized" (required in claim 17); and (iii) the specific molar ratio of each components in said composition (required in claim 18).

Bailey teaches or suggests the advantage of substituting folic acid with the natural isomer of tetrahydrofolic acid or a derivatives including 5-methyl-(6S)-tetrahydrofolic acid for the satisfaction or partial satisfaction of the dietary requirement for the multivitamine preparation; for the accommodation of patient's needs where folic acid bioavailability is poor; and the advantage of providing more choices to health care professionals in recommending optimal levels when a more uniformly absorbed form of folate is widely used (column 6, line 65 thru column 7, line 18).

To incorporate such teaching regarding the use of folic acid derivatives such as 5-methyltetrahydrofolic acid (or 5-methyl-(6S)-tetrahydrofolic acid) into the teaching of Lockett, would have been obvious in view of Bailey who teaches or suggests the advantage of using the natural isomer of tetrahydrofolic acid such as 5-methyl-(6S)-tetrahydrofolic acid in improving poor bioavailability or non-uniformly absorbed characteristic of folic acid.

One having ordinary skill in the art would have been motivated to make such modification to accommodate the needs of those for whom folic acid bioavailability is poor and to accommodate patient's preference where the compliance could be improved with more uniformly absorbed form of folate.

With respect to the limitation of "lyophilized", such determination is well considered within the skill of the artisan since the freeze-drying method is routinely utilized in pharmaceutical formulation art. Since the prior art as a whole fairly teaches or suggests the formulation of said composition in tablet, capsule and liquid, one skilled in the art at the time of applicant's invention would have been motivated to prepare said composition in "lyophilized" or freeze-dried.

Furthermore, optimization of known active ingredients in a composition is well considered within the skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the drug. Hence, the reference makes obvious the instant invention.

Conclusion

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600